

## **Preliminary Communication**

# **Clinical Impressions on the Lower Prevalence of Tardive Dyskinesia in Egypt**

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### **ABSTRACT**

Tardive dyskinesia is abnormal movements that occur as a late complication of neuroleptics. The etiology has not been yet settled. The prevalence of T.D. ranges in different populations from 0.5% up to 56%. Egyptian psychiatrists have observed that T.D. is rarely seen in clinical practice. The possible factors that might underly this clinical impression are discussed. Operational definitions as well as rating scales are supplied to encourage future research in this condition in Egypt.

In recent years, tardive dyskinesia has become a major health problem. Concern over this unfortunate condition has been expressed only during the last two decades with the realization that its prevalence may exceed 10% globally and that the condition may be irreversible. Paradoxically, the prophylactic value of long-term maintenance neuroleptic medication has been well established (Wegner et al., 1979), and tardive dyskinesia has been accepted as an undesirable but occasionally unavoidable price. The price is that it can be incapacitating and debilitating. Research has shown that in some areas of the world TD is not as prevalent as in others. A look at the possible causes for the lower rate in certain areas may provide us with information which can be scrutinized and decrease the rate of TD globally. Tardive dyskinesia, which has also been called "terminal extrapyramidal insufficiency", "complex dyskinesia", and "persistent dyskinesia", is a reasonably well

defined clinical entity that ~~can occur after several weeks or months of~~ antipsychotic-drug treatment but is usually observed only after several years of treatment. In an unknown percentage of cases, the syndrome is apparently irreversible and can be called "permanent dyskinesia". Paradoxically, it may appear for the first time shortly after antipsychotic drug treatment has been discontinued. (American College of Neuropsychopharmacology, 1973).

By definition, this term implies an iatrogenic disease caused by chronic neuroleptic therapy. The early description of this syndrome emphasized abnormal motor movements affecting the face, the so called buccolingual masticatory syndrome (BLM). Later, the syndrome description was broadened to include a variety of abnormal muscular manifestations including choreoathetoid-type movements of the fingers, hands, arms, and feet and flinging or ballistic-type movements, particularly the arms, as well as axial hyperkinesias and diaphragmatic movements resulting in grunting and difficult breathing. As the condition was studied more, the scales for rating the mouthing movements were further refined to include puckering, pouting, smacking, and tongue movements inside the mouth (Klawans et al., 1980).

Although the pathological sequence of changes underlying the development of tardive dyskinesia remains unknown, the hypothesized mechanism leading to the development of tardive dyskinesia is a chemical denervation hypersensitivity of dopamine receptors secondary to neuroleptic blockade. In the normally functioning brain, the basal ganglia facilitate willed movement, when the basal ganglia become deranged they produce movement which is not willed, "an involuntary movement". How this occurs in tardive dyskinesia is not known, an etiologic feature, however, is long-term blockade (Hallett, 1982).

Romero (1982) mentioned that the effects of neuroleptics in producing tardive dyskinesia need not be directly the result of their ability to antagonize the effects of dopamine, but may also be the result of

other specific, but yet to be defined, interactions of the neuroleptics with the cell membrane components.

Evaluation of patients for tardive dyskinesia requires precise assessment tools. There are many different techniques of assessment of tardive dyskinesia. For example instrumentation (including electromyography, pneumatic transducer and ultrasound system for recording movements), frequency counts ( of lip, tongue, and mouth movements), and rating methods using global judgement (Abnormal Involuntary Movement Scale-AIMS) or multi-item rating scales (Tardive Dyskinesia Rating Scale-DRS). The rating scales are the most commonly used tools in tardive dyskinesia and other neuroleptic side-effects research studies. They are universally used and give the most comprehensive picture of tardive dyskinesia (Gardos et al., 1977).

The prevalence of tardive dyskinesia, which has been widely reported in the western countries and North America, varies from about 0.5 % to 56 % (Crane and Smith, 1980). While the diversity of prevalence may be attributable to the different degrees of severity of symptoms used for inclusion criteria, as well as to sex, age, and setting of the population, it is fairly consistent that neuroleptics are considered to be the major causative agents for this syndrome. However, transcultural studies of tardive dyskinesia ( Table I ) yielded lower prevalence in Turkey (Crane, 1968), in Hungary (Gardos et al., 1980), and in Nigeria (Odejide, 1980). It is generally accepted that Turkey is culturally similar to Egypt. Egypt represents a developing country with a population that has different physiological and psychosocial variables. Many Egyptian psychiatric clinicians have the impression that tardive dyskinesia is rarely seen in clinical psychiatric practice. Perhaps this impression has led to the negligence of the study of this syndrome in Egypt. Okasha et al. (1979) carried out the only study published about drug induced extrapyramidal side-effects in Egypt. He assumed that ethnic variations in metabolic factors, such as cerebral amines turnover, may influence the prevalence and nature of EPS. Unfortuna-

tely, the small sample size and the lack of description and quantification of the extrapyramidal symptoms (what symptoms were rated, how they were rated, and if once rated, what would be the definition of the presence of parkinsonism, acute dystonia and akathisia) prevent generalization of the results and unmask the need for valid, reliable and standardized assessment methods of tardive dyskinesia.

**TABLE I**  
**Some Crosscultural Studies of Tardive Dyskinesia**

| Country   | Author & Year               | Number of Patients | Method of Assessment                                            | T.D. %     |
|-----------|-----------------------------|--------------------|-----------------------------------------------------------------|------------|
| U.S.A.    | Crane & Smith<br>1980       | 27 up to<br>10000  | Rating Scales<br>e.g. AIMS,<br>DRS (dyskinesia<br>rating scale) | 0.5-70.4 % |
| England   | Gibson<br>1978              | 374                | Clinical<br>assessment ?                                        | 8 - 22 %   |
| Hungary   | Perenyi & Arato<br>1980     | 200                | AIMS, DRS                                                       | 23.5 %     |
|           | Gardos et al<br>1980        | 122                | AIMS, DRS                                                       | 16 - 44 %  |
| Nigeria   | Odejide<br>1980             | 226                | AIMS                                                            | 9.3 %      |
| Turkey    | Crane & Chase<br>1968       | 40                 | Clinical<br>assessment ?                                        | 7.5 %      |
| Australia | Rey, Hunt & Johnson<br>1981 | 66                 | AIMS                                                            | 44 %       |

Listed below are several features in current Egyptian psychiatric practice that may be relevant in a discussion as to why tardive dyskinesia may not be as prevalent in Egypt :

1. The different physiological and psychosocial variables may play a role in prevalence of tardive dyskinesia in Egypt. The fact that not all the patients on long-term therapy develop this disorder ( Yassa and Ananth, 1981), and the possibility that genetic factors affect drug metabolism may suggest that Egyptian constitution is less vulnerable for the development of tardive dyskinesia. It is relevant to mention that Okasha et al. (1979) assumed that the occurrence of neuroleptic side effects is rather a reflection of personal idiosyncrasy which is in its turn a reflection of the ethnic and constitutional variation in the cerebral turnover of amines.

Crane and Chase (1968) suggested that race and diet may have played a part in the great disparity of findings in a comparative study of tardive dyskinesia between Turkey and the United States. Potts (1982) considered individual and familial variables as predisposing factors known to influence prevalence of tardive dyskinesia.

2. The drug treatment style in Egyptian psychiatric practice may play a minor role. The amount of the dose varies, i.e. small, moderate, and large doses of neuroleptics are given when indicated. It is possible that the type, dose, and frequency of neuroleptic administration differ in Egypt from other parts of the world. There is no evidence yet that a particular type or dose is responsible for tardive dyskinesia ( Potts, 1982; Task Force Report of APA, 1980). However, Klawans et al. (1980) pointed out that the greater the total amount of neuroleptic a patient has received, the higher the risk of severity of tardive dyskinesia.

It may be relevant here to point to the assumption that many patients in Egypt can neither afford the drug expenses for maintenance therapy nor use the more expensive depot neuroleptics. Depot neuroleptics are still less popular in psychiatric practice in Egypt (although they

are becoming more popular recently), and an intriguing and specific association between depot fluphenazine (Csernansky et al., 1982) or depot flupenthixol (Gibson, 1978) and the prevalence of tardive dyskinesia had been reported.

3. The use of antiparkinsonian agent prophylactically for the prevention of extrapyramidal symptoms of neuroleptic therapy might be more popular in Egypt. Some studies reported lower prevalence of tardive dyskinesia with the use of antiparkinsonian agents (Gardos et al., 1980; Asnis et al., 1977), but most of the studies reported opposite results, i.e. concurrent use of antiparkinsonian drugs increases the prevalence of tardive dyskinesia (American College of Neuropsychopharmacology 1973; Task Force Report of APA, 1980).

4. The liberal use of ECT in Egypt in current psychiatric practice is of major importance. ECT is frequently used for acute and recurrent psychotic episodes in Egyptian psychiatric patients. It is employed as a substitute for very high doses of neuroleptics. Price and Levine (1978) reported that ECT may directly benefit an occasional patient with tardive dyskinesia. Also, the use of ECT is recommended in combination with antidepressants in severe depression (APA 1978; Task Force Report of APA, 1980). However, ECT was significantly correlated with increased tardive dyskinesia in some studies (Uharbrand and Faurbye, 1960).

5. Egypt is a developing country with limited economic resources and still other nagging mental health problems and most efforts are directed towards secondary prevention of already detected psychiatric problems. The fact that tardive dyskinesia is still a problem in psychiatric research in well developed countries to the extent that there are major disagreements among experts on the prevalence, course, prognosis, and the promise of effective treatment (Gardos and Cole, 1980) is evident. Thus, psychiatrists in Egypt would be distracted by the more necessitating problems, with their limited resources compared to

developed countries, avoiding research in such ambiguous syndrome where research could be seen, at least in part, as luxurious perfection.

6. Subsequently, this distraction might result in lack of awareness of the tardive dyskinesia problem, (assuming that its prevalence may be a hidden problem) and failure to recognize tardive dyskinesia. Moreover, the complexity of this syndrome, and the unavailability of proper tools for detection, rating scales, as well as trained raters may be contributing factors.

To summarize what has been mentioned, it is possible to consider that tardive dyskinesia as a complication of long-term neuroleptic treatment is still under investigation and exploration of its nature in different populations. The true nature of tardive dyskinesia has not been revealed yet. For identification and isolation of this syndrome, precise and standardized tool of assessment should be used as well as recognized operational criteria. The study of tardive dyskinesia in populations that have lower prevalence might be helpful for clearer understanding of this condition.

Finally, these are preliminary assumptions as regards the impression about tardive dyskinesia and its prevalence rate in Egypt. For future work and possible Egyptian research studies in this area, it would be helpful to use the guiding definitions of tardive dyskinesia and rating scales (appendix 1 & 2).

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#### APPENDIX 1

##### Operational Criteria for Defining

##### Tardive Dyskinesia (Potts, 1982)

1. Involuntary movements involve axial as well as appendicular muscles :

|                  |                                                                                                                 |
|------------------|-----------------------------------------------------------------------------------------------------------------|
| tongue           | Protrusion ("fly catching")<br>rolling ("bon-bon" sign)                                                         |
| lips             | licking, smacking, pouting<br>"rabbit" sign.                                                                    |
| jaws             | Chewing, bruxism                                                                                                |
| facial movements | Opening and closing of mouth,<br>blinking, blepharospasm, puffing of<br>cheeks, grimacing, platysma contraction |
| extremities      | Choreoathetoid movements ("piano<br>playing", foot tapping)                                                     |

trunk

Hip thrusting, rocking

respiratory

Irregular breathing, grunts

pharyngeal

Swallowing, clicking

2. The movements are repetitive, stereotyped, and have a "fluid" character, fixed postures not being a prominent aspect of the syndrome. They disappear during sleep and voluntary effort of the affected region transiently ameliorates the disorder. Conversely, movements of uninvolved parts and stress will aggravate the dyskinesia. Disturbances of muscle tone are not present unless they occur as part of a coexistent syndrome.
3. Involvement of "other motor systems" (cerebellar, pyramidal, etc) is not part of the picture of tardive dyskinesia.

## APPENDIX 2

### Tardive Dyskinesia Scales in Current Use

#### ABNORMAL INVOLUNTARY MOVEMENT SCALE (AIMS)

The AIMS is a 12-item scale designed to record in detail the occurrence of dyskinetic movements. In the development of this scale, the Psychopharmacology Research Branch had the benefit of consulting with many of the scientists who have previously devised rating scales for dyskinetic movements, and of the continuing advice of a formal consultant neurologist (Dr. Roger Duvoisin). One of the units in a PRB collaborative study (St. Paul Ramsey Hospital) had separately undertaken the development of a rating scale and had actively carried out studies with patients showing dyskinetic movements utilizing video-recording techniques. Preliminary versions of the AIMS were used to rate video recordings of patients with dyskinetic movements, and although no formal interrater reliability studies have been conducted, there was relatively good consensus among the group doing the ratings. Because of the great need for an assessment instrument in this field, the scale is being made available to the larger scientific community through the ECDEU Battery, despite the fact that it has not been validated using psychometric procedures.

## EXAMINATION PROCEDURE

Either before or after completing the Examination Procedure observe the patient unobtrusively, at rest (e.g., in waiting room).

The chair to be used in this examination should be a hard, firm one without arms.

1. Ask patient whether there is anything in his/her mouth (i.e., gum, candy, etc.) and if there is, to remove it.
2. Ask patient about the current condition of his/her teeth. Ask patient if he/she wears dentures. Do teeth or dentures bother patient now?
3. Ask patient whether he/she notices any movements in mouth, face, hands, or feet. If yes, ask to describe and to what extent they currently bother patient or interfere with his/her activities.
4. Have patient sit in chair with hands on knees, legs slightly apart, and feet flat on floor. (Look at entire body for movements while in this position.)
5. Ask patient to sit with hands hanging unsupported. If male, between legs, if female and wearing a dress, hanging over knees. (Observe hands and other body areas.)
6. Ask patient to open mouth. (Observe tongue at rest within mouth.) Do this twice.
7. Ask patient to protrude tongue. (Observe abnormalities of tongue movement.) Do this twice.
8. Ask patient to tap thumb, with each finger, as rapidly as possible for 10–15 seconds; separately with right hand, then with left hand. (Observe facial and leg movements.)
9. Flex and extend patient's left and right arms (one at a time.) (Note any rigidity and rate on DOTES.)

10. Ask patient to stand up. (Observe in profile. Observe all body areas again, hips included.)
- \* 11. Ask patient to extend both arms outstretched in front with palms down. (Observe trunk, legs, and mouth.)
- \* 12. Have patient walk a few paces, turn, and walk back to chair. (Observe hands and gait.) Do this twice.
- \* Activated movements.

## الموجز

### انطباعات اكلينيكية من حالات الحركات اللاارادية المتأخرة

حالات الحركات اللاارادية المتأخرة هي عبارة عن حركات غير طبيعية ناتجة عن استعمال المهدئات العظيمة ، وأسباب حدوثها لم تعرف بالتأكيد حتى الآن. وتحدث هذه الحالات بنسبة ٠.٥٪ الى ٥٦٪. وقد أجمع الأطباء النفسيون المصريون على ندرة حدوث هذه الحالات في مصر . وقد ناقشت هذه المقالة أسباب ندرة حدوث هذه الحالة في مصر وأعطت سببيلاً للباحثين ليقوموا بعمل أبحاث تكشف الغموض عن هذه الحالات .

## ABSTRAIT

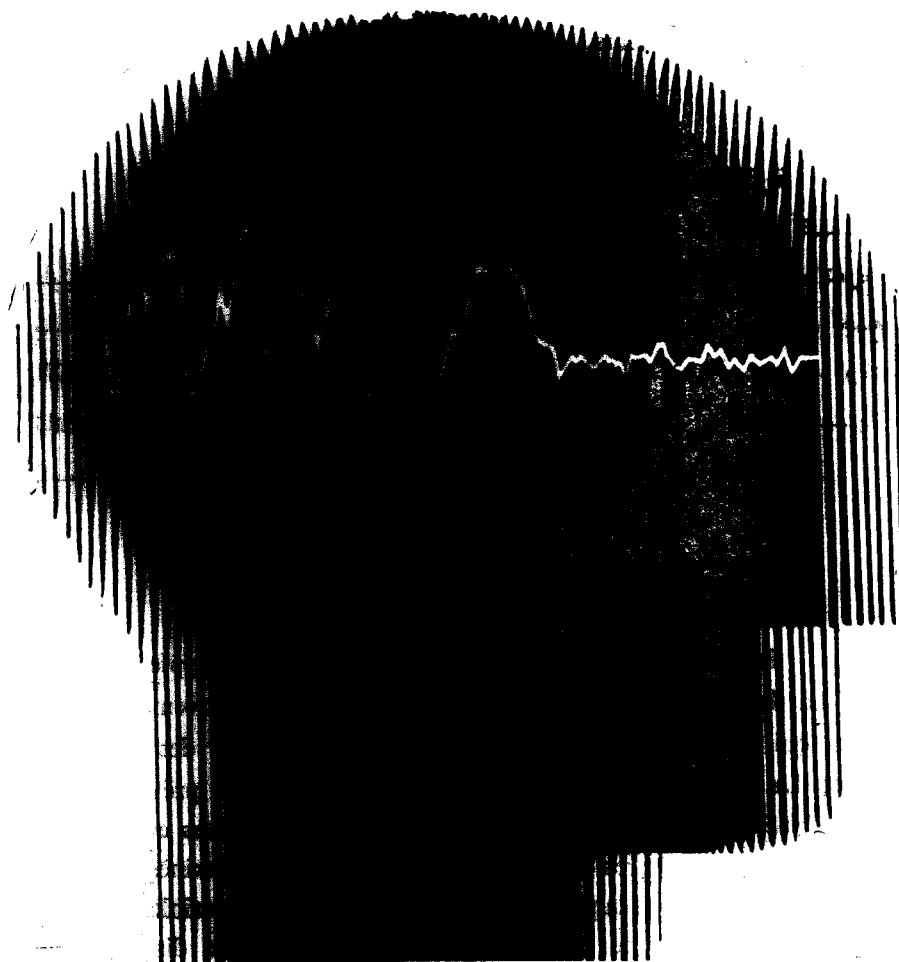
### Impressions Cliniques portant sur

#### la basse prévalence de dyskinésie tardive en Egypte

La dyskinésie tardive comprend la présence de mouvements anormaux qui apparaissent comme une complication tardive des neuroleptiques. La cause réelle n'a pas encore été décelée. La prévalence de la dyskinésie tardive varie dans les différentes populations entre 0.5 % - 0.56%. Les psychiatres égyptiens ont observé que la dyskinésie tardive est rarement vue dans la pratique clinique. Les facteurs possibles qui peuvent être à l'origine de cette impression clinique ont été discutés. Les définitions opérationnelles ainsi que des échelles d'évaluation ont été fournies pour encourager des futures recherches dans cette condition en Egypte.

# Tegretol<sup>®</sup> Geigy

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**C A I R O**

**14. SARAY EL EZBEKIA (EMAD EL DINE)**

**ALEXANDRIA**

**22. EL SHAHID SALAH MOSTAFA**